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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/403,897 02/22/00 BARKAN

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001444 HM22/0621  
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EXAMINER

CANELLA, K

ART UNIT	PAPER NUMBER
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1642

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DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks****BEST AVAILABLE COPY**

<b>Office Action Summary</b>	Application No. 09/403,897	Applicant Barkan et al
	Examiner Karen Canella	Group Art Unit 1642

Responsive to communication(s) filed on \_\_\_\_\_

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 months month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claim

Claim(s) 1-27 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

Claim(s) \_\_\_\_\_ is/are allowed.

Claim(s) 1-27 is/are rejected.

Claim(s) \_\_\_\_\_ is/are objected to.

Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

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## **DETAILED ACTION**

1. Claims 1-27 are pending and examined on the merits.

### ***Claim Rejections - 35 USC § 101***

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-9 provide for the use of an active agent, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

4. Claims 1-9 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

### ***Claim Objections***

5. Claims 19-27 are objected to because of the following informalities: The instant claims are dependent on process claims in an improper format. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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7. Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-9 drawn to the “use of an active agent” are vague and indefinite. The claims are drawn to a method of using an agent, but fail to set forth any active, positive steps that define the claimed method. For purposes of examination, claims 1-9 will be interpreted as method claims.

Claims 1 and 10 recite “active fragments or fractions of any one thereof, active analogs or derivatives of any one thereof...and mixtures of any therefore”. The defining activity of the claimed active agent is unclear. Therefore, the nature of the claimed analogs and derivatives is unclear rendering the metes and bounds of the claims undefined.

Claims 11-17 recite an intended use, but it is unclear how the intended use modifies the claimed active agent. Therefore, most of these claims are duplicates of one another in that the actual product claimed is exactly the same.

Claims 20-25 recite an intended use, but it is unclear how the intended use modifies the claimed pharmaceutical composition. Therefore, most of these claims are duplicates of one another in that the actual product claimed is exactly the same.

The recitation of “an active agent according to claim 1” in claim 19 lacks proper antecedent basis in claim 1. Claim 1 is drawn to a use (method) not a product.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for leptin and leptin fusion proteins, does not reasonably provide enablement for leptin muteins, leptin receptor agonists, active fragments or fractions of anyone thereof, active

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analogs or derivatives of any thereof, and mixtures of any thereof as inhibitors of tumor cell proliferation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. For the leptin to exert its effect of inhibiting the phosphorylation of insulin receptor substrate-1, it must bind to the leptin receptor to activate JAK-2 ( see: Bjorbaek et al, J. of Biological Chemistry, 1997). The instant specification provides only examples and guidance for the use of leptin as an inhibitor of the phosphorylation of insulin receptor substrate-1. Although having an intact leptin protein fused to another protein would have a reasonable expectation of binding the leptin receptor and activating the JAK-2 in the same manner as leptin, one of skill in the art would not know what changes in the leptin sequence could be tolerated by the leptin receptor with respect to JAK-2 activation. Therefore, practice of this invention to the full scope of the claims would require undue experimentation to make and use substances other than leptin or leptin-fusion proteins.

*Claim Rejections - 35 USC § 102*

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claims 1-6, 8-15, 17 and 18 are rejected under 35 U.S.C. 102(a) as being anticipated by Rubinstein (Cytokine, 1997).

Claims 1-6, 8 and 9 are drawn to a method for inhibiting the growth-stimulatory effects of insulin on tumor cell, specifically human breast carcinoma, by the administration of leptin. Rubinstein discloses a method of inhibiting the growth of a human ductal breast carcinoma cell line by the administration of leptin.

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Claims 8-15, 17 and 18 are drawn to leptins and leptin receptor agonists which inhibit human breast cell carcinoma proliferation by inhibiting the growth stimulatory effect of insulin. Rubinstein discloses leptin, which inhibits human breast cell carcinoma proliferation by inhibiting the growth stimulatory effect of insulin.

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 2, 7 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubinstein in view of Jackson (J. of Biological Chemistry, 1998). Claims 1, 2 and 7 are drawn to a method for inhibiting IGF-1, IL-4 or IL-9 from inducing a mitogenic response in tumor cells by the administration of leptin. Rubinstein teaches that the administration of leptin to tumor cells inhibited tyrosine phosphorylation of the insulin receptor substrate-1, while inhibiting cell proliferation. Rubinstein does not teach a method for inhibiting a mitogenic response from IL-4

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stimulation. Jackson teaches the insulin receptor substrate-1 is the main signaling molecule activated by IGF-1, Il-4 in human breast cancer cells. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use leptin as an inhibitor of the mitogenic response to IGF-1 and Il-4. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Jackson on the importance of tyrosine phosphorylation of insulin receptor substrate-1 to the mitogenic signaling pathway induced by IGF-1 and Il-4, and the teachings of Rubinstein on the inhibition of tyrosine phosphorylation of insulin receptor substrate-1 by the administration of leptin..

Claim 16 is drawn to an active agent which inhibits the mitogenic responses of tumor cells to IGF-1, Il-4 and Il-9. Rubinstein teaches leptin as an active agent for use in inhibiting the mitogenic response of tumor cells to insulin. Rubenstein teaches that leptin inhibits the tyrosine phosphorylation of insulin receptor substrate-1. Rubinstein does not teach leptin as an active agent for use in inhibiting the mitogenic response of tumor cells to IGF-1, Il-4 or Il-9. Jackson teaches the insulin receptor substrate-1 is the main signaling molecule activated by IGF-1, Il-4 in human breast cancer cells. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use leptin as an inhibitor of the mitogenic response to IGF-1 and Il-4. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Jackson on the importance of tyrosine phosphorylation of insulin receptor substrate-1 to the mitogenic signaling pathway induced by IGF-1 and Il-4, and the teachings of Rubinstein on the inhibition of tyrosine phosphorylation of insulin receptor substrate-1 by the administration of leptin.

15. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rubinstein and Jackson as applied to claims 1, 2, 7 and 16 above, and further in view of Stephens (USPN 5756461). Claim 24 is drawn to a pharmaceutical composition comprising leptin, for the inhibition of the mitogenic responses in tumor cells induced by IGF-1, Il-4 or Il-9. Rubinstein and

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Jackson teach leptin as a active agent which inhibits the mitogenic reponses in tumor cells induced by IGF-1 or Il-4. Rubinstein and Jackson do not teach a pharmaceutical composition of leptin. Stephens teaches a pharmaceutical composition comprising leptin for the treatment of a type II diabetic patient. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use leptin in a pharmaceutical composition for the inhibition of the mitogenic responses in tumor cells induced by IGF-1, Il-4 or Il-9. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Stephens on the safety and effectiveness of administering leptin or leptin mimetics to humans.

16. Claims 19-23 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubinstein in view of Stephens. Claims 19-23, 25 and 26 are drawn to a pharmaceutical composition comprising leptin for the inhibition of the growth stimulatory effect of insulin on tumor cells and the treatment of human breast carcinoma. Rubinstein teaches leptin as an active agent for the inhibition of the growth stimulatory effect of insulin on tumor cells and the inhibition of cell proliferation of human breast carcinoma cells. Rubinstein does not teach a pharmaceutical composition comprising leptin. Stephens teaches a pharmaceutical composition comprising leptin for the treatment of a type II diabetic patient. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use leptin in a pharmaceutical composition for the inhibition of the mitogenic responses in tumor cells and human breast carcinoma cells induced by insulin. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Stephens on the safety and effectiveness of administering leptin or leptin mimetics to humans.

Claim 27 is drawn to a method for inhibiting tumor cell proliferation in mammals comprising administering to a patient a pharmaceutical composition comprising leptin. Rubinstein discloses a method of inhibiting the growth of a human ductal breast carcinoma cell line by the

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administration of leptin. Rubinstein does not disclose a method for inhibiting tumor cells proliferation in mammals comprising administering a pharmaceutical composition comprising leptin. Stephens teaches a method for the treatment of a type II diabetic patient by administering a pharmaceutical composition comprising leptin. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use leptin in a pharmaceutical composition for the inhibition of the mitogenic responses in tumor cells and human breast carcinoma cells induced by insulin. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Stephens on the safety and effectiveness of administering leptin or leptin mimetics to humans.

#### *Conclusion*

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.  
Patent Examiner, Group 1642

June 16, 2000

  
NANCY A. JOHNSON, PH.D.  
PRIMARY EXAMINER